A cross-sectional analysis of the short-term outcomes of patients receiving prehospital treatment for symptomatic hypoglycaemia in Cape Town

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Part A

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Literature Review

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Background

Prehospital emergency care refers to the management of patients in the out-of-hospital setting, which is provided by Emergency Medical Services (EMS). Two models of such EMS systems exist, namely: the Franco-German and Anglo-Saxon Model. The Franco-German model is focused on the on-scene treatment and stabilisation of a patient, whereas the Anglo-Saxon model encompasses the scoop-and-run concept.[1] The South African EMS context is built on the combination of these models, which provides basic, intermediate and advanced levels of care on-scene. The basic and intermediate life support practitioners provide more of a "scoop-and-run" service, whereas the advanced life support practitioners may encompass a "stay-and-play" methodology. The South African state EMS system thus provides care to a vast array of prehospital emergencies. In the Western Cape context, these emergencies include medical, trauma, inter-facility transfer and rescue incidents. This case load represents 46% of medical emergencies, which commonly includes the management of acute-symptomatic hypoglycaemia.

Acute symptomatic hypoglycaemia (SH) refers to the decrease in blood glucose levels with concomitant decreased level of consciousness and subsequent sympathetic responses or seizues.[2] Currently, various cut-off values for defining acute SH exist in the literature. These values have a range of 3.0mmol/l – 3.5mmol/l.[33] In the South African prehospital context, it is defined as a blood glucose level of less than 3.5mmol/l with the presentation of an altered level of consciousness.[3] Other manifestations include cardiovascular disturbances (such as myocardial infarctions and arrhythmias) and neurological abnormalities (such as transient ischemic attacks and cerebrovascular accidents).[2] SH may also lead to death if left untreated.[2]

In the South African prehospital context, acute SH is classified as priority one call out, where response to such cases should be achieved in less than 15 minutes. Hence various governmental and non-governmental EMS agencies may respond to these callouts when they occur.

The primary underlying causes of SH are Type I and II *diabetes mellitus*. In a 2011 review, it was described that in Africa, Type I diabetes mellitus is poorly

characterised in terms of its aetiology and epidemiology, however did describe a lower prevalence thereof.[6] In a 2008 cross-sectional survey of Type II diabetes mellitus in Bellville, Cape Town, the prevalence of Type II *diabetes mellitus* was 28.2% compared to a global trend of 3.5%.[4, 7] SH may be induced by underlying pathologies, medications or toxins, but is usually a direct result of the injectable insulin alone or concomitantly with oral diabetic treatment agents in Type 1 or II *diabetes mellitus*.[2]

It has been common practice for an EMS crew to leave a patient at home post reversal of acute SH. This decision is based upon patient autonomy post-return of vital signs to within normal parameters, which specifically includes level of consciousness and blood glucose levels > 3.5 mmol/l.[3] Discharge of these patients may also be based upon the patients' wishes to receive further treatment and/or transport. Patients may also refuse further care based on external factors related to personal preferences and socioeconomic conditions. Current protocols as set out by the Health Professions Council of South Africa which governs prehospital emergency care, providers enforce that patients who have experienced an emergency event should be managed and transported to hospital by EMS.[3] However, a patient has the right to refuse transport and treatment.[3] In addition, these protocols are open to interpretation and therefore adherence is variable. These protocols are supposed to be updated every 5-years, but in actual fact have not been since 2006.[3] In terms of the management of acute-SH in the prehospital environment, it does not specifically address management factors, in particular the aspect of discharge post-SH reversal. This protocol only describes oral glucose, intravenous dextrose and glucagon as the agents to be administered. Furthermore, the Western Cape EMS clinical standard operating procedures does not provide any guidelines on the management and disposition of acute SH patients in the prehospital environment.

These factors may lead to the premature discharge of acute SH patients and consequently may result in recurrent episodes.[2] The criteria for leaving symptomatic hypoglycemic patients at home and the appropriateness of the procedure remain controversial; and often crucial associated underlying causes and complications are missed, with repeat episodes of SH potentially risking further morbidity and mortality.[9] Another consideration in this discussion would be the additional burden

placed on an already stretched EMS system. Anecdotally, unnecessary and predictable repeat calls for SH episodes would simply add to this. By leaving these patients at home the causative factors are not determined and managed.

Without knowing the actual effect prehospital discharge of treated acute SH patients has, short- and long-term on patient care and outcomes such as underlying pathologies triggering the SH episode may not investigated and patients run the risk of recurrent episodes.[9] In a recent review evaluating complications of acute SH at a Hospital in Johannesburg, South Africa, it was shown that in almost three-quarters of these patients, the precipitating causes included gastrointestinal abnormalities (20%) and inappropriate treatment (51%).[5]

The role of prehospital emergency care practitioners with extended skills over and above those foreseen by the current protocols is evolving, enabling them to assess and treat patients in the community. These new models of care, including further assessment, triage, and treatment skills for prehospital care providers, have been recommended to help manage ever increasing demands for healthcare. Current evidence concerning safety, effectiveness, and costs to support these changes in practice is lacking.

1. Objectives of Literature Review

The primary objectives of this literature search were to determine:

- the number of patients experiencing their first ever episode of SH
- the short-term outcomes of patients experiencing their first episode of acute SH, and
- re-activation rates of EMS after the index episode, post reversal and discharge.

Secondary objectives included the following:

- determination of hospital admission rates, and
- the provision of follow-up care instructions provided by prehospital care providers prior to discharge.

These objectives were aimed at the prehospital care strategies in various EMS environments to provide a benchmark against which current practice in the Western Cape EMS context could be evaluated.

2. Methodology

2.1 Search Strategy

The following search strategy utilising MeSH terms and keywords as outlined below was used across two medical databases, namely EBSCO Host, Cochrane and Medline:

(prehospital OR out-of-hospital [Title/Abstract] OR paramedic [Title/Abstract] OR ambulance [Title/Abstract]) AND (treatment [Title/Abstract] OR management [Title/Abstract]) AND (symptomatic [Title/Abstract]) AND (hypoclycemia [Title/Abstract]) AND (discharge [Title/Abstract] OR treat-and release [Title/Abstract] OR see-and-treat [Title/Abstract] OR outcomes [Title/Abstract] OR follow-up [Title/Abstract]) OR disposition [Title/Abstract]).

The following search limiters were applied during the search:

- Language: English only
- Articles: Linked full text,abstracts and all other article sources
- Publication Date: 1998 – 2013
- Publication Type: All
- Population Type: Human
- Age Groups: Adults 19+
- Gender: Male and female
- Geography: Open

2.2 Inclusion & Exclusion Criteria

Apart from the search limiters outlined above, the following parameters were also applied: The review includes all electronically indexed eligible articles up to and including 31st October 2013.

Inclusion Criteria:

- Publication Types: Primary and secondary sources, conceptual, anecdotal and clinical opinion
- Population: Male and female patients older than 19 years
- Publication years: 1998 – 2013
- Primary Outcomes: Short-term effects of prehospital discharge post hypoglycemic event reversal
- Secondary Outcomes: Emergency Centre management and outcomes of hypoglycemic patients post discharge in cases of *diabetes mellitus*

Exclusion Criteria:

- Population: Non-humans
- Language: Non-English publications
- Setting: Interventions not carried out in the primary or in-patient setting
- Outcomes: Primary and secondary outcomes that does not report the short-term effects hypoglycemic management

2.3 Quality Criteria

For each search string used, the resulting titles of the articles and abstracts were analyzed in alignment to the objectives of this review (see below). If the title and/ or abstract met the inclusion and exclusion criteria, the full articles were retrieved and read in their entirety. The references at the end of these articles were also reviewed to identify any missed articles. Lastly, the references of this final collection were also examined to identify any additional articles potentially missed during the initial search.

2.4 Search & Screening Results

The search strategy was adjusted within EBSCO Host, Cochrane and Medline and yielded 3833 articles. Advanced limiters were applied using the following key fields: prehospital, out of hospital, Emergency Medical Services (EMS), Emergency Medical Technician (EMT) and Paramedic; and yielded 767 potential articles. Based on the search strategy in correlation with the article titles and repeat hits, 35 were eliminated. A total of 41 articles were screened and 7 were omitted based on the abstract meeting the criteria. A remainder of 34 full-text articles was reviewed and 10 excluded based on the inclusion and exclusion criteria. In conclusion, 22 articles were included for the literature in alignment to the objectives. The following flow diagram (Figure. 1) summarizes the article search and screening process:

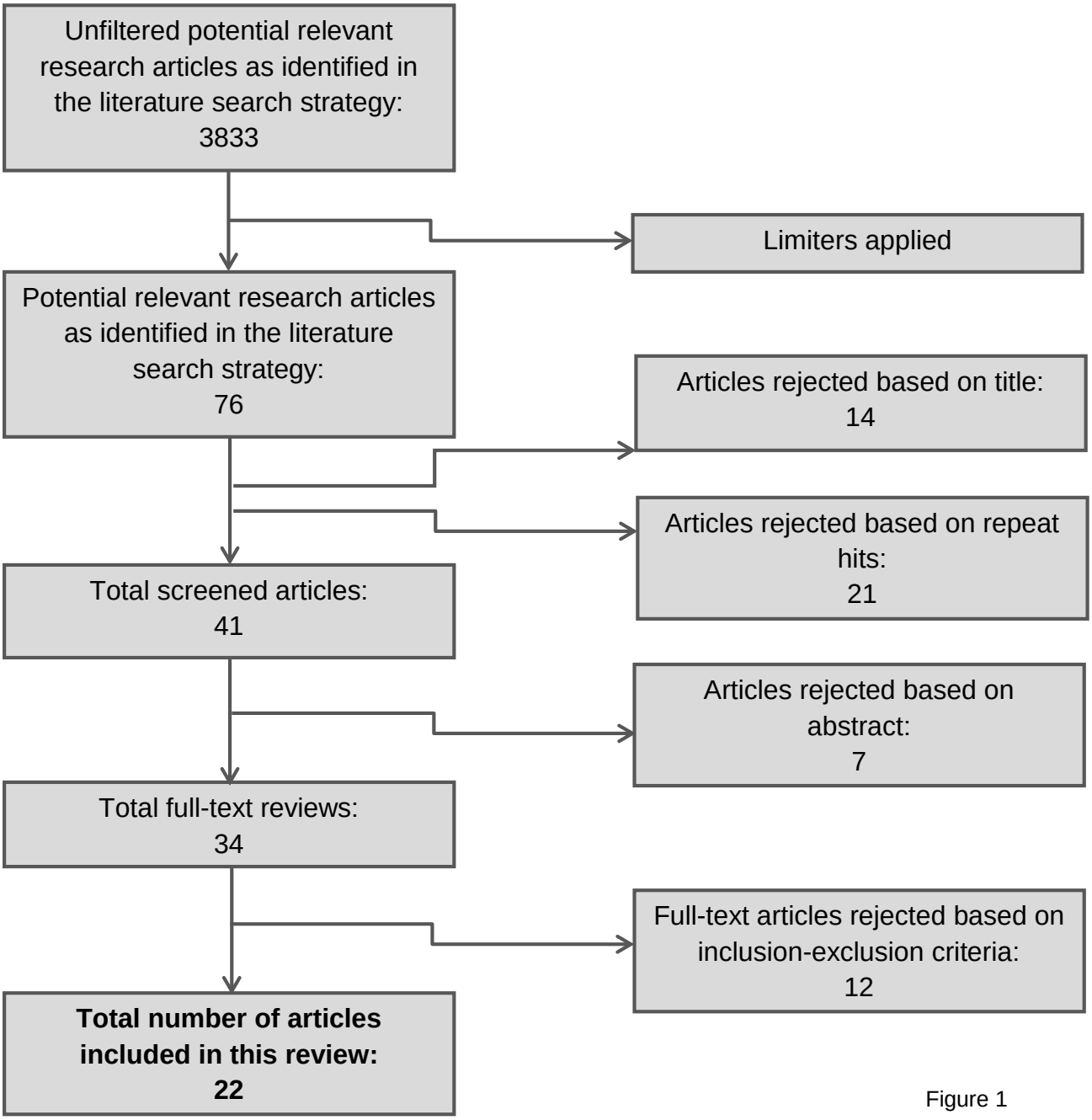

Figure 1

3. Literature Review

Based on the above, Table 1 outlines the sources of literature, the design, key findings and limitations of the 22 included articles, laid out in order of increasing level of evidence and oldest to youngest year of publication:

Table 1: Study Designs and key findings of included papers by year of publication				
Reference Number	**Author, Date & Setting**	**Study Design**	**Key Findings**	**Limitations**
26	Capes *et al,* 2001	Systematic Review	In 26 articles, the relative risk for mortality and stroke post hyperglycaemia was calculated. Patients with hyperglycaemia were shown to be at risk of mortality or stroke.	Heterogeneity
8	Roberts *et al*, 2003	Systematic Review	Showed that out-of-hospital treatment protocols for hypoglycaemic patients were safe in 90% of patients.	Based on out-dated Literature (1990-1999)
14	Donelly *et al,* 2005	Systematic Review	In 267 patients treated with insulin, 45% had subsequent episodes of hypoglycaemia.	Variations in study designs, heterogeneity and inconsistent definitions of hypoglycaemia across studies
27	Nehme *et al,* 2009	Systematic Review	In 3651 potential articles, 24 articles that matched the inclusion criteria showed that 10% dextrose yielded and equal time to normal level of consciousness as compared to 50% dextrose.	Search limited to English articles only No hand-search for articles were conducted
20	Fitzpatrick *et al* 2009 UK EMS	Systematic Review	This review of 23 papers showed an incidence from 0.8% - 23% oral hypoglycaemia inducing agents. Incidents of repeat callout for SH events were between 2-7%.	Only English papers were retrieved. Little high quality papers were found.
24	Frias *et al,* 2010	Systematic Review	82 Cases of adverse events found in literature related to false glucose readings using GDH-PQQ test strips	Voluntary reporting. Small sample size

29	Gerstein *et al,* 2008 Hospital	Randomised Controlled Trial	In terms of standard therapy vs. intensive glucose lowering agents in type 2 diabetes- Primary Outcome: Occurrence of non-fatal MI, stroke or death – Hazard Ratio 0.90 (0.78 – 1.04) 95% CI Secondary Outcome: Death from any cause – Hazard Ratio 1.22 (1.01 – 1.46) 95% CI	Non-standardised dosing strategies.
10	Frye *et al,* 2009 Multicenter Cardiac ICU patients	Randomised controlled trial	Of 2368 cardiac re-vascularization cases, 88.3% of were provided insulin. Of these 9.2% developed multiple episodes of hypoglycaemia.	Hypoglycaemia was not the primary or secondary end-points of this study
21	Steinmetz *et al,* 2006 Prehospital and in hospital	Prospective cohort	Of 139 participants, 6 patients were left at home and required hospital admission through EMS within 48 hours.	Small sample size, patients managed in the prehospital context were managed by physicians
22	Brackenbridge *et al,* 2006 District Emergency Departments & EMS, United Kingdom	Prospective Cohort	In 111 prehospital cases with diabetes, 51% of patients presented with a blood glucose of less than 4mmol/l. Of these, only 27% were transferred to hospital. In the hospital context, 251 cases presented to the units over 12-months with diabetes. 94 Patients presented with hypoglycaemia, which presented with the following underlying pathologies: UTI's (n=6), low GCS (n=4), head injury (n=3), chest infections (n=3), diarrhoea	Hypoglycaemia as a measurable not clearly defined.

			and/or vomiting (n=2).	
18	Strote *et al,* 2007 EMS context, USA	Prospective cohort	203 cases were surveyed out of 402 prehospital hypoglycaemic cases. There was a 16% repeat episode rate of SH, 14% reactivated EMS within 48 hours and 11% required hospitalisation.	Inconsistent study population, large portion of the study populations couldn't be contacted.
23	Voulgari *et al,* 2011 Hospitalised Patients	Method Comparison	Three brands of glucose monitors were evaluated and compared to standard lab measurement. All three-blood glucose monitors under-sensed levels of blood glucose when compared to laboratory measurement.	After calibration of monitors no quality control measures were applied on a daily basis to ensure accuracy amongst monitors. Wide confidence intervals
2	Mechem *et al*, 1998 Philadelphia EMS, USA	Prospective descriptive study	132 Patients enrolled, 103 patients were contacted by telephone, 94 patients had no recurrent SH episodes, nine had recurrent episodes and 8 of these patients were transported to hospital.	Inconsistent telephonic interviews and 22% of the sample population was missed for telephonic interviews.
13	Carter *et al,* 2002	Prospective descriptive study	A total of 157 patients were included in the study, however only 60 were contactable, who refused transport post SH reversal. There was a 31.58% repeat need for healthcare in the transported group compared to 14.63% in the refusal group.	Selection bias due to only 60% of eligible patients being contactable
9	Desouza *et al,* 2003	Prospective descriptive	In 54 patients presenting with hypoglycaemia, cardiac chest pain symptoms were associated	Continuous glucose monitoring systems

	USA	study	with 10 of these cases. In 4 of these 10 cases, ECG abnormalities were detected	may have been inaccurate as it measured interstitial fluid, compared to blood glucose.
15	Henderson *et al,* 2003	Retrospective survey	In 215 patients treated with insulin, 73% presented with hypoglycaemia.	Heterogeneity in study population
16	Holstein *et al,* 2003 EMS Germany	Prospective, population based survey	In 7804 prehospital cases, 215 cases were found to present with SH. Of these 50 patients presented with sulfonylurea induced SH	1173 Cases were excluded due to ethical and inclusions reasons. Cases representative of a single EMS district
17	Leese *et al,* 2003 Ems Academic Hospital, United Kingdom	Retrospective cross-sectional survey	In 8655 cases of diabetes, 160 cases presented with 244 episodes of hypoglycaemia over a 12-month period.	Cases of hypoglycaemia treated outside the EMS or hospital environment were excluded.
28	Cain *et al,* 2003 EMS	Prospective Observational Study	In 220 calls for adult patients with hypoglycaemia, 75 resulted in transport, there were 17 further hypoglycaemic episodes requiring a repeat calls for EMS (22.7%) and three recurrent episodes (4%). Of the 145 calls that did not accept transport, 40 recurrent episodes of hypoglycaemia (27.6%) were reported.	Inability to measure medication involvement in outcomes

12	Raghavan *et al,* 2007.	Clinical Review	Antibiotics (Bactrim, Cephalosporins and Penicillin) known to induce hypoglycaemia	Clinical review, no formal evidence provided
25	Ginsberg *et al,* 2009	Review	Key glucose strip inaccuracies include strip, physical, patient, and pharmacological factors.	
11	Sharma *et al,* 2009	Clinical Review	Hypoglycaemia yet uncommon, found in patients with diabetes on beta-blockers.	Clinical review, no formal evidence provided

Discussion

The management of acute SH includes patient assessment and the administration of anti-hypoglycaemic agents with the aim of returning blood glucose levels to normoglyceamia. Prehospital and in-hospital protocols for acute SH include the treat-and release of patients post-SH reversal. However, the literature showed that the factors and effects, which should be considered, include:

1. Patient autonomy for refusal of transport post-SH reversal
2. Prehospital capabilities to determine underlying SH causative pathologies
3. Medication induced acute SH
4. Increased risks for repeat SH episodes post discharge and repeat EMS callouts
5. Hospital admission post-discharge
6. Follow-up care strategies post-discharge
7. Tools and drugs for prehospital SH management
8. Drug availability in the context of prehospital treatment of acute SH

3.1 Patient autonomy for refusal of transport post SH reversal

Post-acute SH reversal, the patient may elect to seek further medical care which includes hospital admission or may refuse further care. Patient autonomy and legal right to refuse further care need to be taken into consideration if the patient is mentally able to make such a decision. This mental ability is a subjective compound assessment based on both Glasgow coma scale and background mental age, as well as any comorbidities.This may ultimately be in conflict with the patient's welfare. However, decision making ability may be impaired immediately following an episode of SH.[2] One of the hallmarks of severe SH includes an altered level of consciousness, with possible resultant confusion, which may hamper decision making, decrease the ability to reason and present with short-term memory loss.[1] This may constitute a danger to the patient and bystanders. These bystanders

may constitute family members or the public in close proximity to the patient. The lack of reasoning capability may thus result in harmful abnormal behavioural patterns.[2] In a recent psychology review, it was shown that hypoglycaemia may result in aggression, criminality, violence and the ability to inflict self-harm.[31] However, this review was specific in hypoglycemic patients and not applied within the context of other underlying causative pathologies, linked to the prehospital context. An emerging factor was that of treat and release protocols in with respect to prehospital acute-SH patients. However, no published clinical trials were found with specific measurement against the prehospital discharge of acute SH post reversal and the outcomes thereof in specific relation to these protocols. Acute SH is often underestimated by patients' post-reversal. They often may not consider it to be a serious side-effect to diabetes mellitus or representative of underlying pathologies.[8] Thus they may be misinformed in terms of their presenting condition and this may result in negative patient outcomes.

3.2 Prehospital capabilities to determine underlying SH causative pathologies

SH may be disease-, medication-, or toxin induced. The determination of the underlying cause plays a key role in the effective management and secondary prevention of SH and the associated negative outcomes. In a recent review it was found that there was a close association between Type 2 DM and concomitant hypertension, dyslipidaemia and underlying cardiac pathologies and dysrhythmias.[9] The development of acute SH and recurrent episodes thereof may be indicative of the worsening of these comorbidities. A study based on continuous electrocardiogram (ECG) and glucose monitoring during SH reversal showed that 10 out of 54 SH cases showed ECG changes.[9] This may particularly predispose SH patient with underlying cardiac pathologies to dysrhythmias. However, in the *Bypass Angioplasty Revascularization Investigation 2 Diabetes* (Bari 2D) trial it was shown that severe hypoglycaemia was 9.2% more frequent in patients with

underlying cardiac pathologies whilst on insulin therapy for diabetes treatment.[9]

The 2008 ACCORD trial evaluating 10 251 patients with underlying cardiovascular risk and glycaemic control, showed a 35% increase in mortality due to a cardiovascular event.[29] Cardiac medications such as beta-blockers and salicylates has also been shown to predispose cardiac patients to incidents of acute SH, if the patients had underlying Type 2 *diabetes mellitus*. However no evidence was found of acute SH episodes directly causing such cardiac events.[10] It was also further found that acute-SH may mimic transient ischemic attacks, ischemic strokes, arrhythmias and myocardial infarctions.[12] However no articles were found in relation to the long-term outcomes of these presentations and its diagnosis from acute-SH patients managed and discharged in the prehospital context.

Predisposition to acute-SH may also be associated with multiple drug interactions in the treatment of chronic underlying conditions.

A review analysing key aspects of symptomatic hypoglycaemia also showed various diseases which may induce hypoglycaemia (Table 2), however little evidence was found linking these disease causation to acute SH in the prehospital context post reversal.[12]

Table 2: Disease-Induced Symptomatic Hypoglycaemia	
1	Type I *Diabetes Mellitus*
2	Type II *Diabetes Mellitus* – Also associated with hypertension and dyslipidaemia
3	Renal disease
4	Adrenal insufficiency
5	Local & systemic infections
6	Islet cell adenoma
7	Liver cirrhosis
8	Idiopathic hypoglycaemia
9	Autoimmune compromise
10	Pregnancy induced hypoglycaemia
11	Renal glycosuria
12	Hormonal insufficiencies

Adrenal insufficiency can cause hypoglycaemia due to the lack in adrenal hormone secretion such as adrenalin, noradrenalin or cortisol, which plays a vital role in regulating sugar levels.[12] Carcinomas and insulinomas may induce hypoglycaemia, due to the secreted insulin being hampered by tumour cells. Thus insulin secretion is not controlled by glucose and may results in lower than normal blood glucose levels.[12] Liver cirrhosis results in the interference of the structural, intracellular and chemical makeup of the liver. Any change of these components results in inadequate glucose level controls by limiting the ability of gluconeogenesis by the liver.[12] Pregnancy-induced hypoglycaemia may also occur as a result of the increased hormone levels which regulates insulin secretion.[12]

In terms of the above disease-induced causes of hypoglycaemia, no evidence was found internationally and locally evaluating the prevalence and effects of prehospital discharge of acute-SH patients.

In a 2002 retrospective cross-sectional survey in which assessed patient satisfaction post SH reversal in 100 cases in the prehospital setting. In this survey, in which 60 participants were contactable, a

repeat callout rate 14,63% was found. Within this latter group, three patients were diagnosed with chest infection, myocardial infarction and a foot infection respectively.[13] These diagnoses thus suggest a need for further clinical investigations to rule out underlying causes and pathologies which may be represented by an acute SH episode.

In the Western Cape EMS context, there is very little scope for the detection and management of these diseases in the pre-hospital environment. The protraction of these diseases may lead to an increase in morbidity and mortality. Furthermore, it may also result in an increase in healthcare demand in an already resource confined setting.

3.3 Medication induced acute SH

The following medication related factors were found in the literature in terms of acute-SH:

1. Concomitant medication usage
2. Insulin dosage
3. Sulfonylurea adverse effects
4. Antibiotic effects

Acute SH can also be induced by medication use (including hyperglycaemic agents) alone or in combination with multiple medication dosages. Elderly patients may specifically be predisposed to acute SH by multiple drug interactions due to increased tissue sensitivity to concomitant medication usage. In a 2009 case review evaluating drug interactions and renal disease, it was described that renal disease often results in adverse drug reactions and as a result increases the risk of acute SH.[11] The decreased glomerular filtration rate and subsequent creatinine clearance impairs the elimination of multiple renal cleared medications

In the South African prehospital context, callouts are often received for patients on multiple medications due to a number of chronic diseases.

In relation to this, the EMS curriculum for practitioners does not include the interpretation application of these medications.[3] No evidence was found evaluating the presentation of these patients on concomitant medications, acute-SH and outcomes post discharge in the South African prehospital context.

Type I *diabetes mellitus* is primarily managed through the administration of rapid, short or long acting insulin.[31] In cases of Type II *diabetes mellitus* insulin (rapid, short or long acting), sulfonylureas and/or metformin may be administered.[31] A prospective study evaluating the treatment of Type 1 and Type 2 DM in 267 patients showed that 45% of the cases were treated with insulin and had a single or multiple episode/s of SH over a period of time.[14] However, the study duration was short and was unable to ascertain how many dosage adjustments were made in relation to subsequent SH episodes. In another retrospective cross sectional study evaluating the treatment of 215 Type 2 diabetes mellitus patients, it was found that 64% had a subsequent acute SH event, of which 15% were classified as “severe”, defined as a blood glucose level less than 2.5mmol/l and an altered level of consciousness.[15]

Both these studies concluded that post the index SH episode, insulin dosage adjustments had to be made to mitigate subsequent episodes, with hospital admission and monitoring required. These insulin adjustments required close monitoring in relation to blood glucose levels and fasting glucose laboratory investigations. However these studies lacked in providing the adequate timeframe for admission and monitoring required.

A prospective cohort study evaluating the care of prehospital hypoglycaemia found that 4.9% of 213 SH cases were as a result of sulfonylurea use[16], an agent widely used in Cape Town. Another population based dataset analysis investigating 160 cases showed that SH episodes were induced by sulfonylurea and metformin administration in 23 and 69 of cases respectively.[17] These study

outcomes were similar when comparing the results of agents used and the number of acute-SH episodes. It was thus evident that hypoglycaemic agents play a major role in causing SH, especially if injectable insulin is used.

Antibiotics used for the treatment of infections may often cause symptomatic hypoglycaemia by increasing insulin secretion.[12] This may be potentiated in patients with type 2 diabetes mellitus on sulfonylurea treatment. It was also further described that ethanol can precipitate a SH response, as it results in decreased endogenous glucose production and glycogenolysis. Ethanol abuse may particularly be of concern in patients from poor socio-economic status, with resulted malnutrition, decreased endogenous glycogen and glucose stores and resultant recurrent acute SH episodes.

In chronically-ill patients on broad medication usage, dosage and administration adjustments may need to be considered to prevent adverse medication events, such as medication induced hypoglycaemia. These adjustments are dependent on continuous clinical and laboratory investigations which cannot be administered in the prehospital context.

3.4 Increased risk for repeat SH episodes post discharge and repeat EMS callouts

Repeat episodes post SH reversal and prehospital discharge was an emerging theme throughout the screened literature. A follow-up survey comparing outcomes of 203 paramedic treated SH patients in the prehospital setting, showed that 9% (n=19) of cases experienced a repeat SH episode.[15] In another prospective short-term outcome based survey of 103 insulin-dependent SH patients who refused transport after dextrose administration, 91% (n=94) had no recurrent SH episode.[2] However both these studies did not mention the time period within which the repeat SH episode occurred relative to the index episode.

In contradistinction, another prospective cohort study evaluating the outcomes of 220 SH patients treated and not transported in the prehospital context, it was found that of the 34% (n=75) patients who were transported, 22.7% (n=17) had recurrent SH episodes in 24 hours, and 4% (n=3) within 48 hours.[28] However these episodes were not evaluated against special investigations and resultant clinical cause.

As a result of repeat episodes, a fair percentage of acute SH patients will require repeat access to healthcare, usually via the EMS system. In a telephonic survey evaluating patient satisfaction post discharge amongst 41 candidates, it was found that 14.6% (n=6) required repeat access to healthcare for general complaints and 4.8% (n=2) for a recurrent SH episode.[13] In another follow-up survey evaluating prehospital emergency care providers' treatment of hypoglycaemia, it was found that of the 199 cases, 11% (n=8) reactivated EMS through the call centre.[18] These studies took place in the urban USA prehospital context – a context with vast differences as compared to the Western Cape population. These studies did not describe the population-mix and timeframe within which EMS was activated and the specific short and long-term outcomes thereof. These repeat EMS callouts may have significant cost implications for EMS systems and may affect the availability of resources.[19, 20]

All of the studies listed above were conducted outside of Africa. No local studies were found that investigated the issue here. Inconsequently there has also been no local health economic evaluation of this particular type of presentation, practice, repeat episode and discharge.

3.5 Hospital admission post discharge

In a 2006 prospective cohort study assessing 139 prehospital SH patients', it was found that 6% (n=8) required hospital admission post prehospital discharge.[21] However, this study did not identify the

underlying causative factors for hospital admission. In another follow-up survey of 199 discharged SH patients post reversal within the prehospital context, it was found that 16% (n=17) required hospital admission.[18] In this study it was also noted that severe cases of hypoglycaemia were shown to have an 18% recurrence rate within 48 hours. This study showed a link between prehospital discharges of acute SH patients and the requirement for hospital admission in the context of Type II diabetes mellitus

3.6 Follow-up instructions and patient information post discharge

Within the literature search, two criteria for safe discharge emerged which included follow-up instructions and patient information. These were defined together as the provision of effective information in terms of patient education and advice to prevent and management subsequent SH episodes. The key findings included:

1. Educating patients prior discharge reduced SH recurrence
2. In certain cases, the presenting condition may affect decision making capabilities and thus hamper the receipt of information provided
3. Patient education should include medication administration methods
4. Content of follow-up and patient information

Acute SH is related to secondary brain dysfunction. It has been shown that frequent recurrent episodes of acute SH may result in decreased brain function.[18] This may affect a patient's ability to understand follow-up instructions and make coherent decisions on further treatment and transport to hospital for further diagnostic investigations. In one follow-up survey of 203 discharged SH patients, it was found that in 48% (n=97) received follow-up instructions; however no description of the follow-up content and procedures were provided in this study.[18] This study also showed no link between the provision of these instructions and the outcomes thereof. No further evidence relating to the provision

of follow-up instructions was found. In a 2006 prospective cohort study evaluating the use of emergency services by diabetic patients, it was described that patient education with reference to diet and blood glucose control with diabetic agents was lacking.[21] It was further described in this study that the required education in diabetic care was not standard for prehospital care providers, which may have been linked to their scope of practice.[21] Furthermore no evidence was found on the methodology and how to overcome communication barriers with which follow-up strategies should be provided to patients post SH reversal. This is of particular concern in South Africa considering the cultural diversity.

3.7 Tools for Prehospital SH Management

The capability of measuring an accurate blood glucose level must exist. In a 2011 method-comparison study, comparing blood glucose measurements of three brands of blood glucose monitors to that of clinical laboratory analysis within a hospital setting found that these monitors performed poorly at extreme blood glucose values, i.e. resulted in an underestimation of hypoglycaemia and an overestimation of hyperglycaemia.[23] In another review evaluating adverse events associated with false glucose readings, it was described that the following factors affect the accuracy of blood glucose readings:[24, 25]

1. Blood glucose strip accuracy
2. Physical factors (altitude and temperature),
3. Underlying patient constraints (glucometer usage)
4. Concomitant drug therapies

Strip accuracy is affected by strip-to-strip variation, enzyme reactivity, sufficient sample and expiry date. Physical factors include altitude and temperature as biochemical and blood reactivity varies under these extremes. Patient constraints such as incorrect machine coding, inadequate technique and hand washing may affect readings.

Concomitant drug therapies may also cause cross reactivity and hamper blood glucose level readings.[24, 25]

No studies were found with reference to environmental factors affecting the accuracy of blood glucose readings within the prehospital context, thus leading to speculation of its effects. Equipment in the South African prehospital environment in general and Cape Town in particular, is exposed to extremes in temperature and humidity ,which one can speculate may result incorrect blood glucose levels with test strip and glucose monitors.

3.8 Drug availability in the context of prehospital treatment of acute SH

In the South African prehospital context, the following agents are available to treat SH:

1. Oral glucose
2. Intravenous dextrose
3. Glucagon (intramuscular and intravenous)

Intravenous dextrose is a hypertonic solution which increases blood glucose levels in hypoglycaemia and is a source of carbohydrates. Its major function is to prevent the depletion of glycogen stores in the liver, and thus plays a vital role in metabolism. Current protocols suggest the administration of a 50% intravenous dextrose infusion in SH patients.[3] However, a recent review evaluating the efficacy of 10% versus high-concentration intravenous glucose in the out-of-hospital context, it was concluded that 10% intravenous dextrose yielded the same response time to normoglycemia as compared to 50% dextrose.[27] It was also shown that high concentrations of glucose did not match the rate of whole body uptake and may result in recurrent SH episodes. However, this study did not evaluate the correlation to prehospital discharge of SH patient post 50% intravenous dextrose administration and the short- and long-term outcomes thereof.

Current protocols for South African prehospital care providers also includes the administration of oral anti-hypoglycaemic agents in cases where intravenous access cannot be established, or where care is provided by basic life support practitioners. In a recent systematic review, it was concluded that the reversal of SH using oral agents was short acting and often resulted in recurrent SH episodes.[27] However, a major limitation to this review was the determination of timeframes with reference to recurrent SH episodes post administration of oral agents and recovery within the prehospital context.

Glucagon is counter-regulatory hormone acting against insulin and the effects thereof. In a 2011 review evaluating the efficacy of glucagon administration, it was described that glucagon should be the first line of therapy in cases of acute-SH.[32] After intramuscular or intravenous administration, it rapidly mobilises endogenous glycogen and glucose stores. However, one of the disadvantages is that it has a short half-life and is only available to ALS providers. Thus the majority of practitioners in the Western Cape do not have access to glucagon for the management of acute-SH.

Summary of Main Findings

In patients presenting with Acute SH in the prehospital environment, refusal of further treatment and transport to hospital post SH reversal may occur. However, decision making ability in these patients may be hampered by underlying pathologies or the acute effect of the SH. The capabilities and scope of EMS personnel to detect these underlying pathologies are limited. Various medications and pathologies may induce symptomatic hypoglycaemia, and if not correctly managed may result in recurrent episodes. This may be further exacerbated by the type of SH reversal that was applied by the EMS responder. These episodes may result in subsequent EMS callouts and protracted hospital admission rates. Repeat episodes may also increase the risk to these patients in terms of an increased mortality and morbidity. In cases where EMS has discharged these patients, follow-up instructions with reference to

further care in the mitigation of recurrent episodes prior discharge, were found to be inadequate.

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Part B

A cross-sectional analysis of the short-term outcomes of patients receiving prehospital treatment for symptomatic hypoglycaemia in Cape Town

Research Article

Table of Contents

Abbreviations

ALS	-	Advanced Life Support
BLS	-	Basic Life Support
EC	-	Emergency Centre
EMS	-	Emergency Medical Services
HPCSA	-	Health Professions Council of South Africa
ILS	-	Intermediate Life Support
PI	-	Principal Investigator
SH	-	Symptomatic Hypoglycaemia

ABSTRACT

Background*:* There has been a growing prevalence of patients with chronic medical conditions in South Africa, *diabetes mellitus* being one of them. Acute symptomatic hypoglycaemia (SH) refers to decreased level of plasma glucose <3.5mmol/l accompanied by an altered level of consciousness. Prehospital management of such episodes includes reversal by oral and/ or intravenous glucose administration, or intramuscular glucagon administration. Post-reversal, patients may refuse transport to hospital, which may result in recurrent episodes of acute SH.

Methods: A retrospective cross-sectional study design was used. Patient report forms from patients with SH managed prehospitally between May 2012 and September 2012 in the greater Cape Town area were extracted from the Emergency Medical Services (EMS) database. A follow-up survey using a closed-ended questionnaire was administered to these same patients within 7 days post-reversal to evaluate the efficacy of prehospital discharge of SH patients.

Results: A total of 110 eligible patients were identified and telephonically interviewed. It was found that 21(19%) of cases had subsequently died. Of the 89 remaining cases, 30 (34%) reactivated EMS within 7 days of discharge, independent of SH being the chief complaint. In total, 48 (54%) had recurrent episodes of SH within 7 days of discharge by EMS. In 47 (53%) of cases discharged by EMS, no follow-up instructions were provided to mitigate recurrent SH episodes or complications.

Conclusion*:* More than half of patients who received pre-hospital treatment and discharge for SH have recurrent symptoms post reversal by EMS staff, with a third needing to recall the EMS. This would suggest that the current strategy of dealing with such cases needs careful re-evaluation to improve the quality management of this patient population.

1. Introduction

The South African state Emergency Medical Services (EMS) serve as an entry point into the health system for the majority of the population, in particular in previously disadvantaged communities. Over the past decade, there has been a growing prevalence of patients with chronic medical conditions such as heart disease, *diabetes mellitus*, hypertension and infectious diseases.[1] Consequently, amongst the diabetic population, this has resulted in increased EMS callouts for patients presenting with symptomatic hypoglycaemia (SH).

In the South African EMS context it is defined as a blood glucose of less than 3.5mmol/l with the presentation of an altered level of consciousness.[2] There are multiple underlying causes and potentiating factors that may precipitate or exacerbate SH. Over the long-term, SH, especially if recurrent, may lead to increased morbidity and mortality.[3] Even though the three levels of prehospital care (basic (BLS), intermediate (ILS) and advanced life support (ALS)) provide differing levels of intervention, by protocol they are all obliged to transport a patient to hospital unless they refuse. However, anecdotally, this refusal is usually strongly based on the follow-up information provided by the provider. Prehospital management of SH includes immediate reversal strategies, with the paramedic, if available, making the call to discharge post reversal or to transport to hospital, based on the patient's preference. In cases where the paramedic is unavailable, ILS and BLS practitioners may discharge the patient based on the patient refusing further care.

South African prehospital emergency care providers have three pharmaceutical agents available to reverse low plasma glucose levels, namely: oral glucose, intravenous dextrose and glucagon, which is aligned to the national protocols as set out by the Health Professions Council of South Africa.[2,3] The prehospital environment is also limited in terms of diagnostic capabilities. Consequently the practitioner is not in a position to necessarily identify the cause of the SH they are treating. Furthermore, no formal "treat and discharge" protocols existing within the Western Cape EMS.

The aim of this study was to determine the outcome of a sample of adult SH patients who were treated and discharged prehospitally, without taking them on to further definitive care. The primary objective was to determine the number of SH patients who experienced a repeat episode of hypoglycaemia after discharge and made a repeat call to EMS for a subsequent episode of SH within 7 days of the primary event. The secondary objectives were to determine if hospital admission was required subsequent to the index episode of

SH. In addition, this study also assessed if emergency care providers recommended follow-up care and provided patients with information upon discharge.

2. Materials and Methods

2.1 Study Setting

The patients for this study were selected from the Northern, Southern and Western districts of Cape Town, South Africa, in alignment with the Western Cape EMS districts. These patients were identified from the specific Western Cape EMS district database system. This database is updated daily by data capturers from patient care report forms. Data fields include case types, response and mission times, clinical assessment and interventions with disposition methods. Patients with SH as a primary or secondary diagnosis, were selected from this database within the study period in the districts surveyed.

2.2 Methodology

A retrospective cross-sectional study design was used. Patient report forms for patients with a primary or secondary diagnosis of SH between May 2012 and September 2012 were extracted from the EMS database, yielding a convenience sample of 110 consecutive eligible SH cases. A telephonic follow-up survey based on a closed-ended questionnaire was conducted within 7 days of the initial reversal to evaluate the outcome of the prehospital discharge.

This study included all adult SH patients (over 18 years of age), who had a blood glucose level less than 3.5mmol/l and a reduced level of consciousness. Blood glucose levels had to have been determined by glucose monitors (i.e. no colorimetric visualisation methods allowed). Patients needed to have been discharged in the prehospital environment post-reversal using oral and/or intravenous and/or intramuscular hyperglycaemic agents. SH patients outside the Western, Southern and Northern Districts were excluded, as were those managed by the Cape Town Fire and Rescue Services and private sector EMS providers and inter-facility transfers. During the telephonic interview, patients unable to speak and understand English, Afrikaans or Xhosa were excluded, as these represent the most common languages spoken in the Western Cape.

Patient report forms with illegible or absent patient and/or next of kin data were also excluded.

A protocol existed for contacting patients and/ or their next of kin in a systematic manner for up to three tries, after which they were regarded as non-contactable. The telephonic surveys were conducted by the PI and a trained secondary reviewer in English, Afrikaans or Xhosa, dependent on the patient's language preference,. The interviews were conducted off a script that was available in all three languages following forwards and backwards translation for accuracy. The figure below outlines the sampling process:

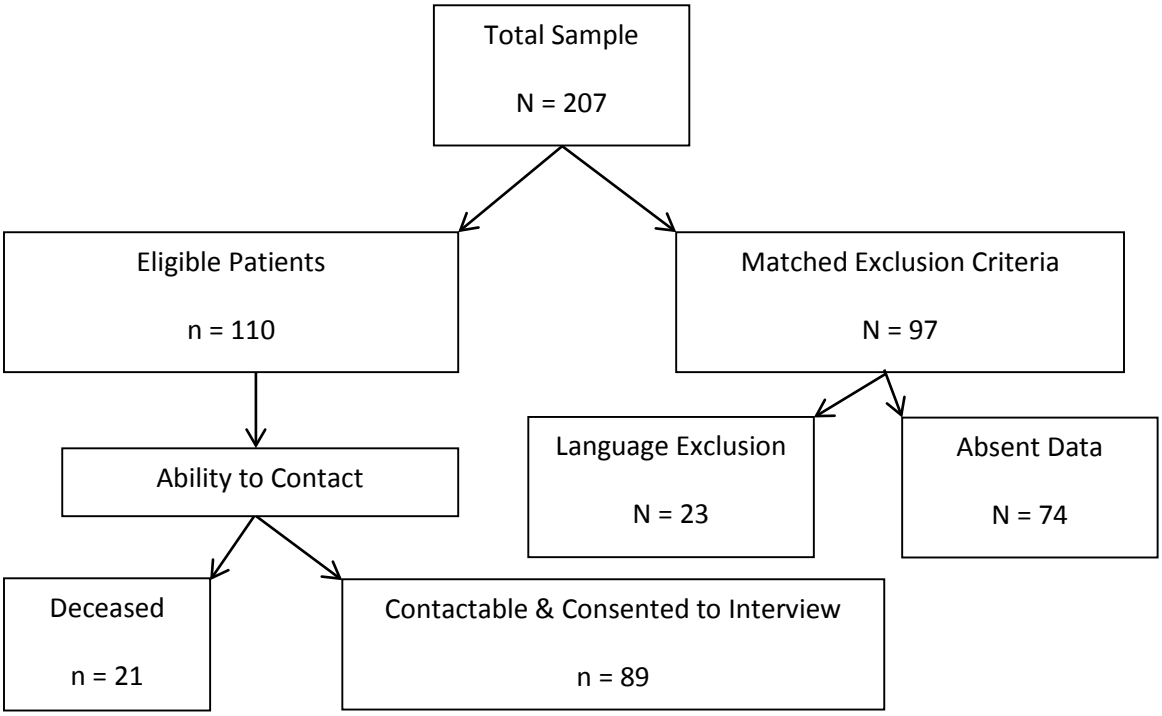

Figure 1: Flowchart of outcome sample

3. Results

110 SH patients were eligible to be included in the telephonic interview. Of note, speaking to third parties, 21 (19%) of the original cases were subsequently found to have died following the initial EMS activation and therefore unavailable for the telephonic survey. The scope of this survey did not allow for the investigation of the presumed causes of death in these patients. The breakdown of cases is shown in Table 1. Of specific interest is the mean age of 56 years (SD=13) for this cohort and that cases were almost equally distributed between males and females.

Table 1 Demographics and characteristics of cases studied

Characteristic	*Value*
N	110
Age (years)*	56 (30-83)
Sex (male/female)	59 (54%)/51 (46%)
Deceased	21 (19%)
Level of prehospital care provided (including deceased cases):	
• BLS	39 (35%)
• ILS	56 (51%)
• ALS	15 (14%)

*Median (range) values

Of the contactable 89 cases, 54 (61%) had subsequent recurrent episode/s of SH within 7 days of discharge by EMS, with 30 (34%) of these cases re-activating EMS in the same time period (Figure 2). This was independent of SH being the chief complaint and motivation for re-activation of EMS.

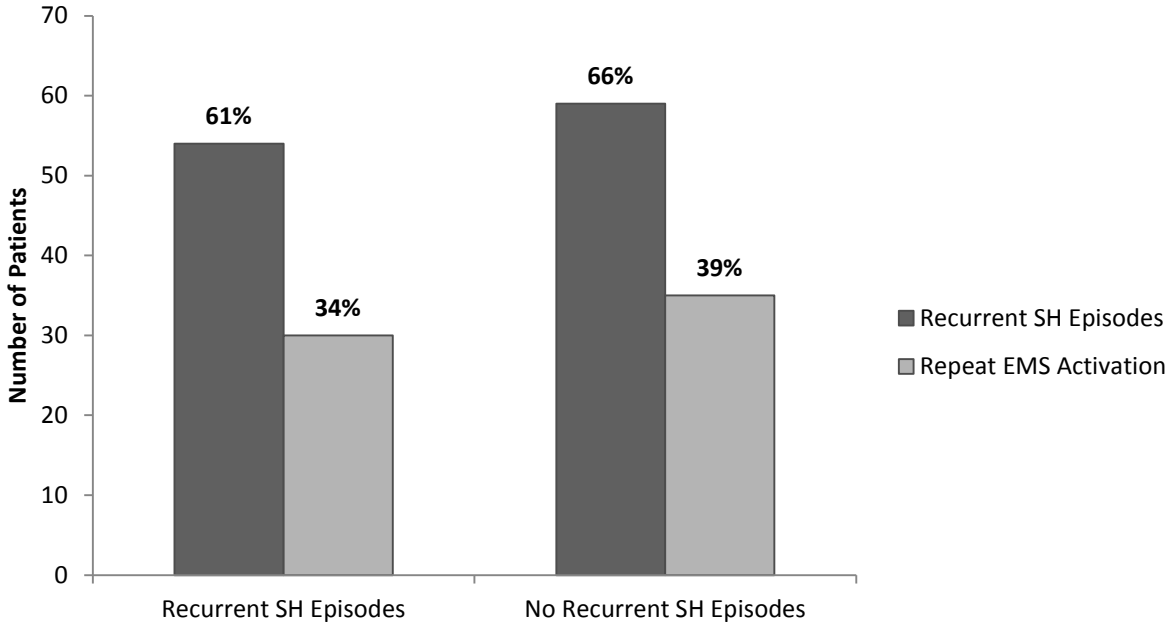

Figure 2: Recurrent SH episodes within 7-days post EMS discharge

Cases with a recurrent episode of SH used the following chronic diabetic medication: : 12(23%) oral diabetic agents, 26(50%) insulin only and 14(27%) were oral and insulin diabetic agents, with 36 of the 89 (41%) eligible patients not using any medication at the time of the incident.

Hospital admission within 7 days post EMS discharge was required for 46 of the 89 SH cases (52%). The reasons for admission included infections (11%); hypoglycaemia

(9%); hypertension (6%); cerebrovascular accidents (6%); and hyperglycaemia (4%), which all may have been linked to chronic underlying *diabetes mellitus*.

Prior discharge post SH reversal, follow-up and patient information was provided to 35 (39%) of patients, and 7 (8%) unable to recall the information or whether this information was provided.

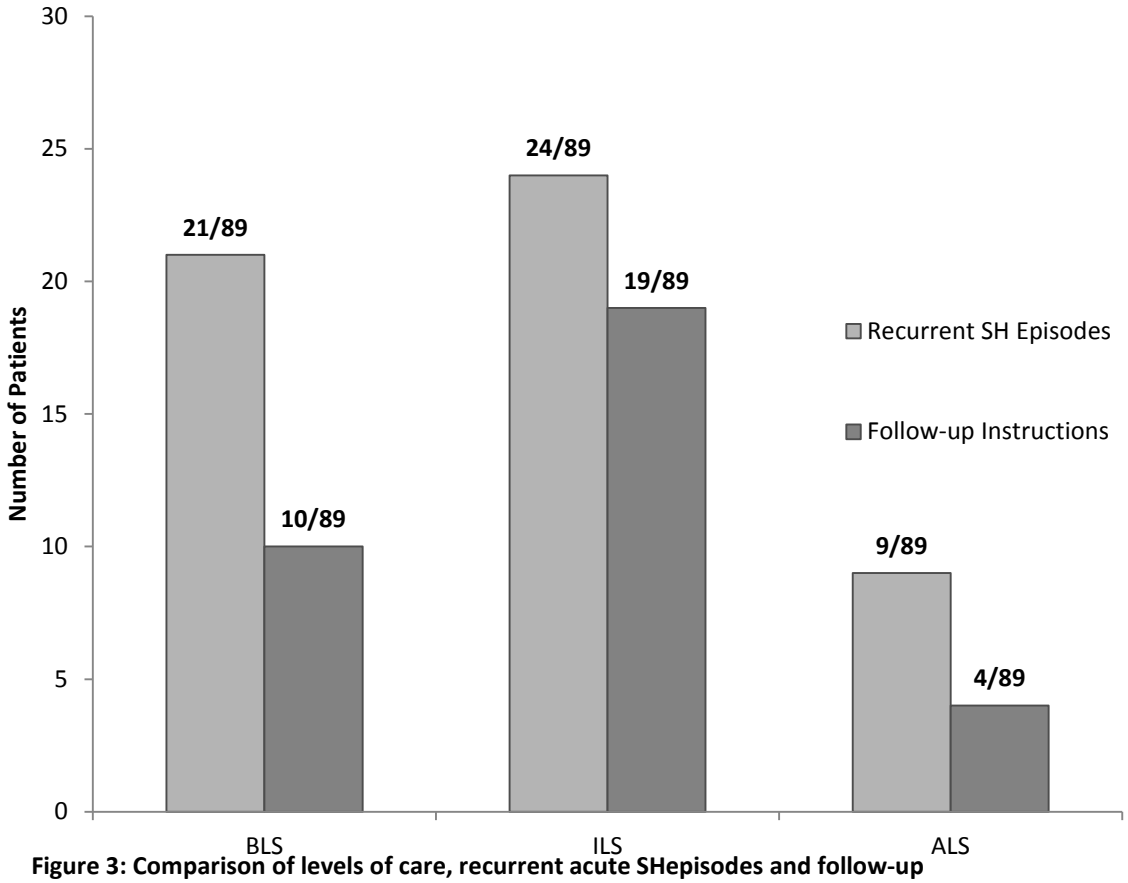

Figure 3: Comparison of levels of care, recurrent acute SHepisodes and follow-up instructions

Figure 3 stratifies the various levels of prehospital care provided, by recurrent SH episodes and provision of follow-up instructions by level of care. Notably it can be seen that there was a related amount of recurrent SH episodes amongst all levels of care. It can also be seen that despite the provision of these instructions, recurrency was still present. Of the 35 BLS, 45 ILS and 12 ALS managed cases; 21(24%), 24(27%) and 9(10%) had recurrent episodes respectively. In the 89 cases, 59(66%) reactivated the EMS system within 7 days of the index prehospital discharge.

It was also found that post-discharge after SH reversal patients had experienced the following abnormal signs and symptoms respectively: headaches with/ without dizziness 30 (27%), increased levels of sweating 15(14%), abdominal discomfort 14 (13%), nausea and vomiting 12 (11%), and weakness and confusion 9(8%).

4. Discussion

Symptomatic hypoglycaemia is considered a potentially serious complication of *diabetes mellitus*. SH may be disease-induced or precipitated by single or multiple medications used in combination.[3] The treatment of prehospital SH is often limited to short term management strategies, with minimal capabilities for the detection of underlying pathologies contributing to the index event.[3, 9]

In this study it was shown that recurrent SH episodes were associated with the reactivation of EMS resources. Deciding to discharge a patient post reversal in the prehospital environment, is often motivated by their refusal of hospital admission and further care.[4] This request cannot be denied on the basis of patient autonomy and legal right. However, more than one third (34%) of cases eventually re-activated EMS within the study period, although the trigger for the second call was not ascertained as it was out of the scope of this study.

The outcomes of this study can be compared to a 1998 prospective descriptive study from the USA, evaluating the short-term outcomes of acute SH patients post discharge. Then it was shown that 91% of cases had recurrent episodes within 72 hours, with 9% of this case re-activating EMS.[4] Though the recurrence rate was higher in the US study, the need to reactivate EMS was higher in our local cohort. Within our prehospital context, this could be attributed to poor socio-economic circumstances and reduced access to definitive care.

Within the Western Cape prehospital context, EMS providers utilize blood glucose monitors as part of their scope of practice. These monitors have inherent limitations as they usually require calibration, a quality assurance step not usually performed.[3] Test strip accuracy may be influenced by expiration and extreme temperature fluctuations and humidity. These factors may lead to under-sensed or over-sensed blood glucose levels, which influences treatment and discharge strategies.[7]

In cases where intravenous access cannot be established or BLS care was provided, oral hyperglycaemic agents are administered. These agents are short acting and may take a longer period of time to achieve the desired blood glucose level, thus potentiating neurological fallout.[11] This can be linked to the outcomes of this study where 24% of the BLS cases experienced recurrent episodes, as oral glucose may have resulted in inappropriate premature discharge. Current South African prehospital

ILS and ALS protocols for the management of acute SH patients include the administration of intravenous dextrose 50%, intramuscular or intravenous glucagon and oral anti-hypoglycemic agents.[13] The current dextrose dosage results in a faster time to restore blood glucose levels to normoglyceamia. High concentration dextrose may induce hyperglycaemia in the short term and/ or result in renewed hypoglycaemia in the longer term.[16] This phenomenon may also have played a role in this study in which 27% and 10% of ILS and ALS cases respectively experienced recurrent episodes of SH. An additional treatment is the biosynthetic form of glucagon. It stimulates the release of glucose from the liver by the process of glycogenolysis, thus increasing blood glucose levels.[11] However it is dependent on adequate endogenous glucose stores, which may already have been exhausted due to repeated episodes of hypoglycaemia, starvation, extensive liver damage or adrenal insufficiency.[11] These factors are often unknown to prehospital providers.

Within the Western Cape EMS system, SH patients are primarily discharged prehospitally if they refuse further care, or show normalisation of blood glucose levels and a return to their pre-episode level of consciousness on-scene. The current prehospital discharge practice is not sensitive to risk mitigation, as they are not tempered by the underlying causative factors. Recurrent SH episodes may also be linked to medication usage, with specific emphasis on self-administered insulin and dose related errors.[7] Common oral agents such as the sulfonylureas, metformin and antibiotics have been shown to potentiate SH.[8, 9, 10] The increased rate of subsequent SH episodes and EMS reactivation shown in this study, may have been linked to inadequate dosing of these agents (73% of cases were using anti- hyperglycaemic agents), and concomitant medication usage. The data in this study also showed that recurrent SH was especially evident in patients using insulin (48%) when compared to oral diabetic agent use only (27%) . This outcome is supported by a recent systematic review, in which 47% of a group of 267 patients who had been treated with insulin, presented with recurrent SH episodes.[18]

Participants in the study period reported abnormal signs and symptoms post-discharge. These included headaches with/ without dizziness, increased levels of sweating, abdominal discomfort, nausea and vomiting, and confusion. This compares favourably to possible serious underlying pathologies, often independent *diabetes mellitus* precipitating the index event.[15, 17]

Current levels of prehospital care with the Western Cape EMS include Basic, BLS, ILS and ALS, with the vast majority of practitioners only having BLS and ILS training. In this study 39% and 53% of acute SH patient were managed by BLS and ILS practitioners respectively, with a combined SH recurrency of 51%. This may have posed a significant risk to patients due to the limited capabilities of this practitioners.[12, 14]

In terms of follow-up instructions and patient information, this study showed that all levels of EMS personnel provided similar follow-up instructions, resulting in similar levels of recurrence (21% and 27% respectively). Thus, patient outcomes may have been independent of follow-up instructions. In addition, prehospital care providers omitted the provision of follow-up instructions or patient information prior to prehospital discharge, post SH reversal, in a large proportion of patients. It was also shown that in certain cases where these instructions were verbally provided to the patient, they were unable to recall such instructions. What role the manner in which the provider provided the information played, or whether it is associated with the poor cognitive states post SH reversal remains uncertain.[5] Decreased levels of plasma glucose results in sympatho-adrenal nervous system stimulation and subsequent further drops in glucose may result in an increase in mortality and morbidity. Consequently, multiple recurrent SH episodes increase the risk for neurological deficits with resultant long term local and systemic morbidities.[6] Furthermore these neurological deficits may have affected cognitive function and thus the patient's ability to reason and make adequate decisions around further care strategies.[7] This is not usually considered in the prehospital discharge process. It thus becomes a concern in this study population, in which 8% of cases experienced weakness and confusion post-discharge.

Follow-up care instructions play a key role in the safe disposition and discharge of patients, particularly in the prehospital context. These instructions should ideally be in writing, evidence-based and vetted against patient outcomes (Appendix A). It should also include standardised information cards for the patient or bystanders to identify early signs and symptoms of recurrent SH. These criteria should also be linked to differential underlying pathologies which may flag serious comorbidities, upon which the patient or bystanders may appropriately act upon. However, a disadvantage of this may be linked to the inability of patients to interpret this information due to the longstanding effects of *diabetes mellitus* e.g. inadequate vision..

Subsequent to repeat activation of EMS post initial discharge, 52% of the study patients required hospitalisation. In a similar study conducted in 2008, 199 acute SH patients were followed up post reversal after prehospital discharge In this group 16% required hospital admission.[15] It was also noted that severe cases of hypoglycaemia were shown to have an 18% recurrence rate within a 48-hour period.

In a recent cohort study it was shown that patients with recurrent SH had extended hospital stays, increased morbidity and an increased need for specialised nursing.[19] In another recent review of costing impact per patient presenting with hypoglycaemia in Spain, it was described that a single episode may cost in excess of €3500 (≈ZAR 52 500 at current exchange rates).[20] Thus, repeat SH episodes may prove to be very costly for patients and funders. A major compounding factor is that of quality of life for the patient in terms of long-term effects of recurrent SH episodes. The scope of this study did not include the evaluation of the health economics the premature SH discharge, however the results may be extrapolated within its effects.

Though the study was not designed to further explore the causative factors leading up to the death, a high proportion of SH cases initially discharged were found to be have died upon telephonic follow-up. One would also have to assume that a number of those patients who did not respond to the telephonic challenge themselves might have died. In which way the original disposition strategy may have contributed remains speculative in specific relation to prehospital discharge post SH reversal and the detection of underlying causative pathologies and should form the basis of further investigation.

5. Limitations

The study population was limited to three Metropole EMS divisions, thus the data cannot automatically be extrapolated to the remainder of the Western Cape population as a whole. However, as detailed, these divisions are fairly typical and major differences at least within the Western Cape are not expected. In terms of the data collection, inconsistencies may have existed in relation to data entry. A major constraint in this was the identification of pure SH cases, due to often ambivalent data. A further limitation was the exclusion of data from Fire Services, private EMS agencies, Inter-hospital transfers and other first responders. There was also a degree of recall bias during the telephonic interview; however this was limited by putting in place the 7-day time limit within which it was conducted. The detailed analysis of time sequences in

both prior and post- index SH episode relative to underlying co-morbidities was not possible. In terms of the deceased cases, a detailed analysis of causal pathways and associations to the index SH episode was not possible with the study methodology employed.

With reference to the need for hospital admission post SH reversal, the diagnosis provided by patients or relatives may not have been on the causal pathway from the index SH episode. The diagnostic capabilities and provision of patient follow-up information by the prehospital care providers may also have been limited by levels of adequate training.

This study also lacked a control group measuring the rate of recurrent visits to Emergency Centres and EMS callouts, for those patients managed in the Emergency Centres within the included EMS districts. Thus it is difficult to determine if the recall or TTH rate was average high or low for this service.

6. Conclusions

The determination of the underlying causative factors is a vital part of the treatment of SH. Even in this small review, 52% of patients required hospitalisation following their initial treatment and prehospital discharge. Therefore, effective treat and release protocols should be developed to prevent repeat episodes, reduce the repeat call out rate for SH episodes and mitigate risks These protocols should demonstrate a systematic approach to the management of acute SH to all levels of prehospital care providers. The management strategies should include effective history taking and diagnostic procedures to identify underlying pathologies. A key criterion here would include risk stratification tools. These mitigation strategies will also reduce the development and progression of co-morbidities and would have to be developed in conjunction with hospital-based Emergency Centres that would deal with these patients. Currently, no evidence exists on the long and short-term outcomes of the implementation of such strategies. This is of importance in the Western Cape and South Africa as a whole, as resources in both the prehospital and inhospital context are limited.

Comprehensive and understandable information is an important treatment component when considering prehospital discharge of any patient. Effective patient and relative information cards should be developed and implemented to enable the patient and their

family to make informed choices on their further care. These cards should include pertinent information such as emergency contact numbers, disposition options and symptoms of a recurrent SH episode. Importantly it should be easy to understand and available in the locally relevant languages.

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Appendix A – Prehospital Acute SH Discharge Instructions

General Information

The prehospital care provider has treated you for an acute episode of hypoglycaemia (low blood sugar levels). Your sugar levels were corrected through intravenous and/or oral glucose agents. He/she has tested your sugar levels and found it to have improved to normal levels. **Please follow the instructions below:**

Follow-up Care

- Please contact your doctor as soon as possible and inform him/her that your blood sugar levels had dropped below the normal levels.
- Consult with your doctor in terms of follow up care in relation to your diabetes.
- Limit all physical activity over the next 24hrs. These activities include sports, driving or any other activity where a sudden loss of consciousness may harm yourself or others.
- Eat something as soon as possible and maintain regular meals.
- Abstain from alcoholic beverages or recreational drugs over the next 24hrs.

Should you experience any of the following symptoms please call 10177 from a landline or 112 from your mobile phone:

- Unusual weakness, numbness or inability to move a leg or arm
- Excessive drowsiness, confusion or slurred speech
- Visual disturbances
- Fainting
- Seizures
- Nausea or vomiting
- Headaches
- Any other symptoms which may be similar or worse than previous problems

DO NOT SIGN THIS FORM IF YOU WANT TO BE TAKEN TO HOSPITAL FOR FURTHER CARE

Incident Number: _____

Date: _____

Patient Name & Surname: _____

Patient Signature: _____

Paramedic: _____

Paramedic Signature: _____

Witness Name & Surname: _____

Witness Signature: _____

Comments:

_____

_____

_____

_____

Part C

Cross-sectional analysis of the short term outcomes of patients receiving prehospital treatment for symptomatic hypoglycaemia in Cape Town

Research Proposal

TABLE OF CONTENTS

1. Abstract

Background:
Acute symptomatic hypoglycaemia (SH) is a condition, managed in the pre-hospital environment by emergency care providers. Post-reversal, patients often refuse further treatment and transport.

Purpose:
To retrospectively determine the number of adult symptomatic hypoglycaemic patients who required further intervention post-reversal following pre-hospital discharge in the Western Cape Metropole.

Objectives:
- To determine the number of SH patients who experienced a repeat episode after discharge.
- To determine how many repeat calls were made to EMS for a subsequent episode of SH within 7 days after the primary event.
- To determine if hospital admission was required subsequent to the index episode of SH.
- To assess if follow-up care strategies were provided by pre-hospital emergency care providers upon discharge.

Study Design:
A retrospective cross-sectional design.

Setting:
This study will take place in the pre-hospital context in three Cape Town EMS districts.

Study Population:
SH patients treated by pre-hospital emergency care providers.

Study Sample:
Convenience sampling will be employed, which will retrospectively identify a minimum of 110 consecutive SH patients.

Data Collection Methods:
The Western Cape EMS database will be queried and applicable patient report forms extracted. A telephonic interview will be conducted using a closed-ended questionnaire.

Statistical Methods:
Basic statistics, including proportions and corresponding confidence intervals will be determined per question.

2. Introduction

Acute symptomatic hypoglycaemia refers to decreased plasma glucose levels, which may result in sympathetic nervous system stimulation and/or altered levels of consciousness. Decreased plasma glucose results in decreased glucose supply to cerebral tissue; which may manifest as central nervous system neuro-pathologies including confusion, dizziness, irritability, hallucinations, focal impairment with resultant coma and eventual death. Furthermore, this results in the stimulation of the sympatho-adrenal nervous system which manifests as sweating, palpitations, anxiety, and hunger.[1]

The prognosis of patients presenting with acute symptomatic hypoglycaemia is dependent on the determination of the causative factors with early effective and efficient increase in plasma glucose levels. In the pre-hospital setting, emergency care providers have three pharmaceutical agents available to reverse low plasma glucose levels, namely: oral glucose, dextrose and glucagon. Incorrect or unidentified causative factors of hypoglycaemia may result in deleterious effects on the outcomes as currently no treat and release protocols exist within the Western Cape Emergency Medical Services. This study will evaluate the effectiveness of pre-hospital discharge within the context of patients presenting with acute symptomatic hypoglycaemic episodes post reversal.

2.1 Literature Review

Pre-hospital emergency care providers play a pivotal role in the detection and management of symptomatic hypoglycaemic (SH) patients. The key focus should be the identification of causative factors, reversal of the symptomatic hypoglycaemic state; and safe and efficient patient disposition strategies.

SH may be induced by a number of diseases (see Table 1).

Table 1

	Disease-Induced Symptomatic Hypoglycaemia
1	Type 2 Diabetes – Also associated with hypertension and dyslipidaemia
2	Renal disease
3	Adrenal insufficiency
4	Local & systemic infections
5	Islet cell adenoma
6	Liver cirrhosis
7	Idiopathic hypoglycaemia
8	Autoimmune compromise
9	Pregnancy induced hypoglycaemia
10	Renal glycosuria
11	Hormonal insufficiencies

Type 2 diabetes serves as a major contributing factor for the induction of SH. In a recent review it was described that in Sub-Saharan Africa, the number of people with Type 2 diabetes will double between the year 2000 and 2030 with a death rate of 40-80/ 100 000 people nationally.[2] Globally, the prevalence of type 2 diabetes in the year 2000 was 2.8% and 6.9% undiagnosed type 2 diabetes globally, which indicates the poor investigation of presented signs and symptoms amongst these patients.[3] Type 2 diabetes is commonly associated with hypertension, dyslipidaemia and underlying cardiac pathologies.[3] Patients with type 2 diabetes may average 16 hypoglycaemic events annually which is closely related to inadequate dosage and administration of medications such as metformin, insulin and sulfonylurea.[1] There is a close association between diabetes and cardiac disease. Cardiac patients receiving beta-blockers and salicylates as a means to mitigate dysrhythmias and atherosclerosis, are predisposed to incidents of SH (Table 2). [11, 12] In a recent review, it was described that renal disease often results in adverse drug reactions and as a result induces SH.[4] This is caused by the impairment of medication elimination due to a decrease in glomerular filtration rate and creatinine clearance.

Adrenal insufficiency may also induce SH due to decreased secretion of adrenalin and noradrenalin from the adrenal medulla.[5]

In chronic conditions where glycogen stores are depleted, the patient will require constant dextrose infusions and monitoring; otherwise a simple reversal may result in metabolic acidosis, respiratory failure or hemodynamic instability.[8]

SH can also be caused by medication use alone or in combination with multiple medication dosages (see Table 2).

Table 2

	Medications prone to inducing Symptomatic Hypoglycaemia alone or in combination
1	Metformin
2	Insulin
3	Sulfonylurea
4	Antibiotics
5	Ethanol
6	Beta-blockers
7	Salicylate

Secretagogues such as sulfonylureas are common causes of SH in type 2 diabetics.[9] Sulfonylurea-induced SH is correlated to inadequate caloric intake, pharmacological interactions and initial exposure, and thus careful monitoring of these patients are required.[9] Antibiotics used for the treatment of infections may often cause symptomatic hypoglycaemia by increasing insulin secretion.[7] This may further be potentiated in patients with type 2 diabetes sulfonylurea treatment.

A recent study has shown that in South Africa the prevalence of alcohol abuse occurs at 6%.[10] This indicates an increased potential for alcohol induced SH. Ethanol causes potent SH responses which results in decreased endogenous glucose production and glycogenolysis, thus presents with life-threatening consequences.

When dealing with the pre-hospital treatment of SH, a third aspect to consider is the means of diagnosis. Blood glucose monitors are the mainstay diagnostic modality;

however they have a number of shortfalls. These include calibration errors, test strip accuracy correlated to expiration and external environmental factors. In a recent hospital study evaluating the accuracy of blood glucose monitors, it was found that these monitors often over-sensed or under-sensed blood glucose readings.[13] Thus, episodes of hypoglycaemia may be underdiagnosed and those of hyperglycaemia over diagnosed, which could be extrapolated to the prehospital setting as the similar blood glucose monitors are used.

Glucose monitors have varying sensing levels toward different sugars thus may produce stable levels of the incorrect sugar type. Ketones may also cross-react on strips resulting in false positive or false negative results. These factors may be mitigated against in hospitals as a result of on-going observation and monitoring as well as recourse to laboratory checks.

In the South African pre-hospital context, pharmacological management of SH includes the administration of oral glucose (oral hypoglycaemic agents), intravenous dextrose or glucagon.[14] Oral hypoglycaemic agents may result in recurrent SH episodes. In a recent systematic review its was shown that the administration of oral hypoglycaemic agents may result in recurrent SH episodes.[15]

In the South African pre-hospital context, a major component of EMS systems are Basic Life Support providers, where oral hypoglycaemic agents are the only pharmacological SH agents which may be administered within their scope of practice. Oral hypoglycaemic agents can also be administered by Intermediate and Advanced Life Support practitioners in the absence of intravenous access for the administration of dextrose. In the South African pre-hospital context, current protocols include the administration of 50% intravenous dextrose.[14] Studies have shown that high concentrations of dextrose may result in an excessive increase in blood glucose levels to hyperglycaemic levels.[19, 20] This may pose as a potential risk to SH patients and lead to a false sense of security where patients may refuse transport to definitive care with resultant pre-hospital discharge by emergency care providers. This may also result in rapid blood glucose level decrease with recurrent SH.

Effective management of SH patients in the pre-hospital context includes safe and efficient disposition strategies. Patients presenting with SH in the pre-hospital environment often prefer discharge with no hospital admission post SH reversal.[16,17,21] Pre-hospital discharge of SH post reversal has been shown to be safe in primarily in Type 1 diabetic patients as they had received formal patient education which may prevent recurrent SH episodes.[18, 23]

Pre-hospital discharge of SH patient post-reversal may present with inherent complications. In a recent prospective case series study it was concluded that pre-hospital discharge post-reversal led to an 8% complication rate.[23] Pre-hospital discharge post reversal has been shown to be effective in conditions where adequate discharge information is provided to patients to prevent recurrent SH episodes.[24,25] In a recent follow-up survey evaluating outcomes of 203 patient post discharge within 48 hours, it was concluded that there were 8% recurrent episodes, 5% repeat Emergency Medical Service callouts and 11% hospital admissions upon recurrent callout.[26] Pre-hospital discharge post SH reversal may expose patients to clinical risk due to incorrect diagnosis, pharmacological treatment and ineffective referral pathways with patient education and advice provided by pre-hospital emergency care providers.

2.2 Motivation for Study

South African pre-hospital emergency care is a complex field which has rapidly advanced over the past decade, and serves as an entry point into the health system for patients, especially in previously disadvantaged communities. Over the past decade there has been a growing incidence of patients with chronic medical conditions such as heart disease, diabetes mellitus, hypertension and infectious diseases, thus increasing the number of patients accessing Emergency Medical Services.

There is an increased incidence of callouts are received for patients presenting with symptomatic hypoglycaemia.SH is a complex condition with varying causes which may be induced by underlying causes and inefficient management may potentiate these causes thus increasing morbidity and mortality. Pre-hospital management of SH includes reversal strategies and discharge post reversal of SH. Currently no

discharge protocols exist within the context of pre-hospital discharge of SH patients post-reversal due to a lack of evidence based on the outcomes of these patients, although performed on a daily basis. This study will identify the outcomes of these patients post-discharge following the current practice of pre-hospital discharge by emergency care providers.

2.3 Research Question

Are subsequent interventions required to treat further episodes of symptomatic hypoglycaemia in adults who were treated for the same in the pre-hospital context by Emergency Medical Care providers and subsequently discharged in the field?

2.4 Aim

To retrospectively determine the outcomes of adult symptomatic hypoglycaemic patients who were treated and discharged pre-hospitally.

2.5 Objectives

- To determine the number of SH patients who experienced a repeat episode of hypoglycaemia after discharge.
- To determine how many repeat calls were made to EMS for a subsequent episode of SH within 7 days after the primary event.
- To determine if hospital admission was required subsequent to the index episode of SH.
- To assess if follow-up care strategies were provided by pre-hospital emergency care providers upon discharge.

3. Methodology

3.1 Study Design

A retrospective cross-sectional study design will be used as it will provide individual characteristics, effect of risk factors and information with regard to an event outcome. Patient report forms from symptomatic hypoglycaemic patients managed by pre-hospital emergency medical care providers will be extracted from the EMS

database. These forms will be collected from the Western Cape Emergency Medical Services Metropolitan Area – Northern, Southern and Western Districts. A minimum of 110 patients will be interviewed, matching the inclusion criteria. Patients will be contacted via telephone to conduct a telephonic interview. If a patient is unreachable after the first attempt, a second attempt will be made 24 hours later. However, if the patient remains unreachable, they will be excluded from the study. Patients will also be excluded if no or illegible telephone numbers occur on the patient care report form. A follow-up survey using a closed-ended questionnaire (Annexure 1) will be applied to evaluate the short-term outcomes (7 days) efficacy of pre-hospital discharge of hypoglycaemic patients' post-reversal.

3.2 Study Population

The Western Cape Provincial mortality due to diabetes was 100 per 100 000 population as at 2006, with higher prevalence rates among Coloureds, Indians and Whites.[27] These population groups are mostly located in the Northern, Southern and Western regions. Collectively these regions account for most of the Western Cape's population due to its dense residential occupancies. The Western Cape Emergency Medical Services (EMS) often responds to SH patients as a result of poor glucose control with diabetes. The Western Cape EMS (Metropole region) responds to approximately 10 000 incidents monthly, of which a percentage includes SH patients with poor glucose control; with underlying diabetes. In relation to the population distribution, a great percentage of these incidents occur in these regions.

The patients for this study will selected from the Northern, Southern and Western regions of the Western Cape in alignment to the EMS districts. These patients will be identified from the Western Cape EMS district data system. Patients who presented to EMS in these districts with symptomatic hypoglycaemia as a primary or secondary diagnosis, which post-reversal and discharged pre-hospitally will be selected for this study.

3.3 Sampling

Convenience sampling will be employed, which will retrospectively identify a minimum of 110 SH patients who had presented to the three metropolitan districts and was discharged post-hypoglycaemic reversal. A target sample of 110 SH cases will be aimed for to compensate for possible attrition. These patients will be contacted and interviewed within 7 days of the initial callout. The process will be conducted until a total of 110 patients that have met the criteria to be interviewed have been reached across the three EMS districts.

3.3.1 Inclusion Criteria

This study will include all adult symptomatic hypoglycaemic patients (over 18 years of age) who presented to the Western Cape EMS Metropolitan Area – Western, Southern and Northern Districts. Symptomatic criteria would include patients with a blood glucose level less than 3.5mmol/l and with an altered level of consciousness. This study will only include patients where blood glucose levels were determined by glucose monitors. Accu-Chek® Active monitors will be used (standard issue within the Western Cape EMS), as these monitors are self-calibrated upon insertion of coding chip which accompanies each specific test strip package. Expiry dates of test strips are regularly checked by pharmacists upon issue to practitioners. These test strips are only valid for a three month period upon opening of the package. The study will include patients matching these criteria in relation to primary pre-hospital management by a basic, intermediate or advanced life support pre-hospital emergency medical practitioners. Only adults (over the age of 18) will be included. This study will only include patients with the above criteria, who were discharged in the pre-hospital environment.

2.3.1. Exclusion Criteria

This study will exclude symptomatic hypoglycaemic patients outside the Western Cape EMS Metropolitan Area – Western, Southern and Northern Districts. Symptomatic hypoglycaemic patients managed by the Cape Town Fire and Rescue Services; and private sector Emergency Medical Service providers will be excluded. Symptomatic hypoglycaemic patients managed by primary facilities requiring inter-

facility transfer via EMS to secondary or tertiary facilities omitted. Patients with asymptomatic hypoglycaemia or low blood glucose in the absence of an altered level of consciousness will not be included. During the telephonic interview, patients unable to speak and understand English, Afrikaans or Xhosa will be excluded. Patient report forms with illegible or absent patient and/or next of kin data will also be excluded. Upon introduction in the telephonic interview, the investigator will seek consent from the patient and given the option to withdraw from the study at any point during questioning. Patients not providing consent or choosing to withdraw from participation will also be excluded from this study.

3.4 Data Collection and Management

Data for this study will be collected from the Western Cape EMS district data capture tools, patient report forms and telephonic interviews (through questionnaires). The Western Cape EMS – Northern, Western and Southern Districts' monthly incident statistics will be retrieved through databases. These incident statistics will identify all diabetic incidents for these regions, hence identifying the pre-hospital diabetic incidents. This data will provide specific dates, times and location of incidents in order to retrieve patient care report forms (Annexure 2). Patient care report forms will be collected from the Western Cape EMS central data store. Patient care report forms will be used as a tool to retrieve patient contact details to conduct the telephonic closed-ended questionnaire. Illegible entries within patient care report forms will be excluded. A record will be kept with regards to the number of patients thus excluded. Illegible or inconsistent entries will likewise be excluded from the study and reported upon. To avoid duplication of data, each SH case will be removed from the data sheet and the corresponding patient care report form.

The patients' past medical and medication history will be captured from the patient report form and confirmed through the telephonic questionnaire. The EMS level of care data will also be captured.

The telephonic survey will be conducted in English, Afrikaans or Xhosa dependent on the patient's language preference, as these are the most common languages in the Western Cape.[31] The interview will be conducted by the principal investigator to cater for English and Afrikaans participants, and a secondary interviewer to conduct

the Xhosa survey if required. This secondary interviewer will be trained by the principal investigator with the aid of simulated interviews. To ensure accurate translation, forwards and backwards translation will be applied. If a patient is unreachable after the first attempt, the patient care report form will be put aside and a second attempt will be done within 24 hours. However, if the patient remains unreachable, they will be passed-over. If the telephone details provided are that of a third party, an attempt will be made to get the telephonic contact details of the patient, however if contact cannot be made due to any reason telephonically in this 24 hour period, the patient will be passed over.

Each completed questionnaire will be bound to a copy of the corresponding patient report form with copies of district statistics which will be held in lever-arch files secured in a lockable metal cabinet at the Western Cape EMS – College of Emergency Care. Inability to contact patients during the telephonic interview sessions will be noted and reasoning captured and analysed. Prior administration of the telephonic questionnaire, the procedure shall be explained to the patient.

Throughout the data collection phase duplicate copies of these files and compact discs will be made with corresponding updated data. These duplicate data files will be stored with the principal investigator.

Data from the questionnaires will be retrieved and captured onto Microsoft Excel 2010, where it will be backed up on external USB storage devices and remote storage server which will only be accessible to the principal investigator and supervisors of this study. The captured data will also be encrypted and password protected to limit access to the principal investigator and supervisor upon request.

The retrieved data will be analysed in specific relation to the aims and objectives of this study.

3.5 Timeline

2011		• Formulation of research proposal
2012	Jan	• Formulation of research proposal
	February	• Submission to Divisional Research Committee
	March	• Submission to Surgical Divisional Research Committee • Submission to UCT Human Research Ethics Committee • Approval – Institutional – Western Cape EMS • Data collection and capturing
	April	• Data Collection and capturing
	May	• Data Collection and capturing
	June	• Data analysis
	July	• Thesis write-up & submission – Study Supervisor
	August	• Feedback – Study Supervisor – Apply corrections • Final submission for grading
	Sept	• Feedback
	Oct	• Feedback
	Nov	• Feedback

4. Statistical and Data Analysis

4.1 Sample Analysis

The primary analysis method in this study will be the calculation of the proportion and corresponding confidence interval for the questions listed in the telephonic questionnaire data capture sheet. The required sample size was therefore based on this proportion and achieving the desired precision in the 95% confidence interval. A sample size of 93 valid responses will be sufficient to achieve a 10% precision in the estimate of the population proportion.

4.2 Data Analysis

Microsoft Excel™ 2010 will be used to capture the data and STATISTICA™ version 10 will be used to analyse the data.

The primary objective of the study is to determine the number of SH patients who experienced a repeat hypoglycaemic episode after discharge in the pre-hospital environment.

Summary statistics will be used to describe the variables. The distributions of variables will be presented with histograms and/or frequency tables. Medians or means will be used as the measures of central location for ordinal and continuous responses and standard deviations and quartiles as indicators of spread.

Relationships between two continuous variables will be analysed with regression analysis and the strength of the relationship measured with the Pearson correlation, or Spearman correlation, if the continuous variables are not normally distributed. If one continuous response variable is to be related to several other continuous input variables, multiple regression analysis will be used and the strength of the relationship measured with multiple correlation.

The relationships between continuous response variables and nominal input variables will be analysed using appropriate analysis of variance (ANOVA). The ordinal response variables will be compared to a nominal input variable, non-parametric ANOVA method will be used. For completely randomized designs the

Mann-Whitney test or the Kruskal-Wallis test will be used and for repeated measures the Wilcoxon- or Friedman tests will be used.

The relation between two nominal variables will be investigated with contingency tables and likelihood ratio chi-square tests. A p-value of $p< 0.05$ will represent statistical significance in hypothesis testing and 95% confidence intervals will be used to describe the estimation of unknown parameters.

5. Ethical and Legal Considerations

Primarily, patient autonomy and confidentiality will be maintained throughout the phases of this study. Verbal consent will be obtained telephonically as per the Helsinki protocol. All patients will be informed of the background, aims and objectives of this study (Annexure 3). Permission shall be obtained and documented (Annexure 4) from the Western Cape Department of Health EMS to obtain data from their internal databases and patient care report forms. These will only be made available to the principal investigator and supervisors of this study. All participants will be made aware of this facility. Interviews conducted by participants including the principal investigator will complete a patient confidentiality form (Annexure 5). All interview data will only be made available to the principal investigator, supervisors and the Western Cape Department of Health.

During the telephonic interviews, patients may be dissatisfied with services rendered by the Western Cape Department of Health EMS practitioners. These patients will be directed to the specific Continuous Quality Improvement EMS official within their district.

6. Limitations

This study will only investigate SH patients managed in the pre-hospital setting by the Western Cape Department of Health – EMS practitioners in three districts. Patients managed by Cape Town Fire & Rescue Services, and private sector EMS providers in these and other districts will be excluded, therefore limiting external validity.

The recruitment process of SH patients into this study may affect internal validity. Selection bias may occur as a result of patient pass-over instances. This may also occur as a result of patients refusing to partake in the study, illness, death, migration or missing data.

This study will only include cases where Accu-Chek® Active glucose monitors were used as it is standard issue to Western Cape EMS personnel. Colourmetric blood glucose levels determination using test strips will be excluded and other brands of glucose monitors. As a result of this, bias toward Accu-Chek® Active glucose monitors may be displayed.

The study survey will not be conducted in all eleven official languages of South Africa; hence some patients will be excluded from the sample group.

A non-validated closed-ended questionnaire will be used to survey patients. Closed-ended questions will enable the allocation of quantitative methods which will allow for statistical interpretation. These types of questions are more specific, thus similar meanings during interview responses will be interpreted. However, the questionnaire may result in leading or suggestive answers wanted by the investigator. Closed ended questionnaires also do not allow room for further discussion and emergence of themes related which may contribute to the aims and objectives of this study.

7. Resources

7.1 Available Resources

	Description	**Source**
1	Statistical Services	Centre for Statistical Consultation, Stellenbosch University UCT and US Joint Division of Emergency Medicine
2	Travel Services	Principal Investigator
3	Telephone communication	Western Cape Department of Health EMS – Contact Centre
4	Internet access and email facilities	Principal Investigator
5	Computer including Microsoft Word and Excel	Principal Investigator
6	Printing and copying	Principal Investigator

7.2 Budget

Budget				
February – December 2012				
Item	**Description**	**Unit cost**	**No. of Units**	**Total cost**
1. Communication	Phone services			R0.00
	Internet and Email services	R100.00/ month	8	R800.00
2. Specialized services	Bio statistical Services	R185.00/hr	10	R1850.00
3. Office supplies, printing & reproduction for data collection	Printing	R0.40 / page	1000	R400.00
4. Travel to sites	Travel cost	R3.61/ km	500	R1805.00
Total Direct Costs				**R5855.00**
Indirect Costs (12%)				**R702.60**
Total				**R5557.60**

8. Reporting and Implementation of Results

Upon conclusion of the study, the results will be made available to the Western Cape Emergency Medical Services and the Health Professions Council of South Africa. These results will serve as a platform for further investigation into the discharge of SH patients post-reversal in other similar prehospital environments. Hence, this will encourage the review of current practice in the management and discharge of SH patient's post-reversal.

It will also be made available to the University of Cape Town's Department of Emergency Medicine and other Paramedical training institutions, locally and nationally. Dissemination to pre-hospital emergency care providers' training institutions will raise awareness and responsiveness to the management and discharge of these patients.

The outcomes of this study will serve as the basis for future research within the context of pre-hospital discharge for symptomatic hypoglycaemic patients within the Western Cape. This study will demonstrate the safety and efficacy of pre-hospital discharge of hypoglycaemic patient's post-reversal by emergency care providers.

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ANNEXURE 1

PATIENT QUESTIONNAIRE

Incident Date: _____ Incident Time: _____

Dispatch No: _____ Shift: _____

Patient Report Form No: _____ Patient Age: _____

Patient Gender: _____ Patient Language: _____

Ambulance Diagnosis: _____

Prehospital Level of Care (circle): | B | I | A |

Interviewer: _____ Interview Date: _____

	Question		
1	Was this your first episode of low blood sugar levels when you activated the Ambulance Service?	**Yes**	**No**
2	What diabetic medication are you utilising? (please √)	**Oral agents only**	**1**
		Insulin only	**2**
		Oral agents & insulin	**3**
		None	**4**
3	Did you have to go to the hospital within 7 days after discharge by EMS?	**Yes**	**No**
4	If yes to question 4, what was the hospital diagnosis?		
5	After discharge by EMS, did you experience any of the following within 7 days of discharge? (please √)	**Nausea & vomiting**	
		Headaches or dizziness	
		Increased sweating levels	
		Abdominal discomfort	
		Weakness & confusion	

6	Do you have a glucose monitor at home?	**Yes**	**No**
7	When you experienced any of the above, did you or your family check your glucose (sugar) levels with your glucometer?	**Yes**	**No**
8	If yes to question 7, was it low, high or normal? (please √)	**Low**	**1**
		Normal	**2**
		High	**3**
9	Upon discharge by the ambulance staff, did they provide you with follow-up instructions after your first episode of symptomatic hypoglycaemia should you have felt ill again? (please √)	**Yes**	**1**
		No	**2**
		Unable to recall	**3**
10	Did you have to call the ambulance service within 7 days after discharge by the Ambulance Services?	**Yes**	**No**
11	Post discharge by the ambulance personnel, did you have another episode of symptomatic hypoglycaemia within 7 days?	**Yes**	**No**

Reason for inability to contact:

	Reason	**Please √**
1	Contactable	
2	No answer	
3	Wrong number	
4	Refused	
5	Not available	
6	Ill/ Hospital	
7	Deceased	

Inclusion Criteria Check List to PRF:

	Criteria	**Please √**
1	Northern/ Western/ Southern District	
2	Adult > 18yrs	
3	GCS < 15/15	
4	Discharged by EMS post reversal	

ATTACH TO CORRESPONDING COPY OF PATIENT CARE REPORT FORM

ANNEXURE 2

DATA CAPTURE SHEET

															Symptoms post EMS Discharge										
No	Incident Date	Incident Time	Dispatch No.	PRF No.	Shift	Age	Gender	Language	Prehospital Level of Care	First Episode	Contactibility	Type of Diabetic Medication Use	Hospital Admission within 7 Days	Hospital Diagnosis	Nausea & Vomitting	Headaches or Dizziness	Increased Sweating Levels	Abdominal Discomfort	Weakeness & Confusion	Home Glucose Monitor	Re-assessment of glucose at home using a glucometer	HGT Levels at home (Low, Normal or High)	EMS Follow-up Instructions provided	Activation of EMS within 7 days of discharge	Re-current SH within 7 days of EMS discharge	Meets inclusion Criteria
1	1/2/2012	16:30	10146	546321	D	47	M	E	I	Y	1	2	Y	Pneumonia	√	√	√	√	√	Y	Y	1	1	Y	Y	√
2																										
3																										
4																										
5																										
6																										
7																										
8																										
9																										
10																										

ANNEXURE 3

PATIENT INFORMATION SHEET FOR TELEPHONIC INTERVIEW

TITLE OF THE RESEARCH PROJECT:	**Pre-hospital Discharge of Hypoglycemic Patients Post-Reversal**
REFERENCE NUMBER:	**BLYMOH001**
PRINCIPAL INVESTIGATOR:	**Mohamed Ridhaa Booley**
ADDRESS:	**University of Cape Town – Joint Division of Emergency Medicine**
CONTACT NUMBER:	**072 672 2223/ 021 938 6730**

The following will be read to the patient over the telephone

Good Day

My name is Mohamed Booley. Do you speak and understand English, Afrikaans or Xhosa?

I would like to invite you to participate in a research project that aims to look at the current practice of discharging patients directly after intervening during an episode of low blood sugar to which the ambulance crew responded.

Also, your participation is entirely voluntary and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the Health Research Ethics Committee (HREC) at the University of Cape Town.

This study will consist of a questionnaire, comprising of 11 questions which will evaluate your experience post discharge by ambulance personnel and will take approximately 5 minutes to complete.

Please note that this call is record for record purposes and all personal information will be kept confidential.

Patient Information Checklist		
1	Do you understand that which I have explained to you?	
2	Do you consent to partake in this study	

Mohamed R. Booley

Principal Investigator

ANNEXURE 4

INSTITUTION AUTHORIZATION

TITLE OF THE RESEARCH PROJECT:	**Pre-hospital Discharge of Hypoglycemic Patients Post-Reversal**
REFERENCE NUMBER:	**BLYMOH001**
PRINCIPAL INVESTIGATOR:	**Mohamed Ridhaa Booley**
ADDRESS:	**University of Cape Town – Joint Division of Emergency Medicine**
CONTACT NUMBER:	**072 672 2223/ 021 938 6730**

To whom it may concern,

I …….. representing the Western Cape Government Department of Health-Emergency Medical Services under his/her capacity as **Director: Western Cape Emergency Medical Services** - herewith authorize that this study be conducted in light of the principal investigator retrieving patient care report which will provide critical data to enable the administration of a telephonic interview for hypoglycaemic patients discharged in the pre-hospital setting. I also herewith authorize the principal investigator to make use of the Western Cape Emergency Medical Services contact centre in order to conduct a telephonic survey to meet the aims and objectives of the research project.

It is accepted by the principal researcher that all legal and ethical aspects of this study will be considered and mitigated as outlined in the presented study proposal and adhered to at all times.

Signed at (*place*) .....…….. On ( ) ……..…….. 2012.

....

Signature Print Name in full

ANNEXURE 5

PATIENT CONFIDENTIALITY – TELEPHONIC INTERVIEWER

TITLE OF THE RESEARCH PROJECT:	**Pre-hospital Discharge of Hypoglycemic Patients Post-Reversal**
REFERENCE NUMBER:	**BLYMOH001**
PRINCIPAL INVESTIGATOR:	**Mohamed Ridhaa Booley**
ADDRESS:	**University of Cape Town – Joint Division of Emergency Medicine**
CONTACT NUMBER:	**072 672 2223/ 021 938 6730**

I _____ understand and acknowledge that:

1. I shall respect and maintain the confidentiality of all discussions, deliberations, patient care records and any other information generated in connection with individual patient care, risk management and/or peer review activities.

2. It is my legal and ethical responsibility to protect the privacy, confidentiality and security of all medical records, proprietary information and other confidential information relating to the Provincial Government Western Cape Department of Health – Emergency Medical Services and its affiliates, including business, employment and medical information relating to our patients, members, employees and health care providers.

3. I shall only access or disseminate patient care information in the performance of my assigned duties and where required by or permitted by law, only with the express approval of my supervisor or designee. I shall make no voluntary disclosure of any discussion, deliberations, patient care records or any other patient care, peer review or risk management information, except to persons authorized to receive it.

4. I agree to discuss confidential information only in the work place and only for job related purposes and to not discuss such information outside of the work place or within hearing of other people who do not have a need to know about the information.

5. I understand that the law specially protects psychiatric and drug abuse records, and that unauthorized release of such information may make me subject to legal and/or disciplinary action.

6. My obligation to safeguard patient confidentiality continues after my termination of services with the principal investigator

I hereby acknowledge that I have read and understand the foregoing information and that my signature below signifies my agreement to comply with the above terms. In the event of a breach or threatened breach of the Confidentiality Agreement, I acknowledge that the University of Cape Town, its partners and affiliates involved in this study may, as applicable and as it deems appropriate, pursue disciplinary action via internal or external legal processes.

Signed at (*place*) .....…..…….. On ( ) ……...…….. 2012.

....

Signature Print Name in full

Part D

UNIVERSITY OF CAPE TOWN

Health Sciences Faculty
Human Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6338 • **Facsimile** [021] 406 6411
e-mail: shuretta.thomas@uct.ac.za

04 May 2012

HREC REF: 160/2012

Mr M Booley
c/o Dr T Welzel
Department of Surgery
Emergency Medicine

Dear Mr Booley

PROJECT TITLE: CROSS-SECTIONAL ANALYSIS OF THE SHORT TERM OUTCOMES OF PATIENTS RECEIVING PREHOSPITAL TREATMENT FOR SYMPTOMATIC HYPOGLYCAEMIA IN CAPE TOWN.

Thank you for responding to the issues raised by the Faculty of Health Sciences Human Research Ethics Committee in your letter received on 3rd May 2012.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year till the 15th May 2013

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/research/humanethics/forms)

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC. REF in all your correspondence.

Yours sincerely

Wesley Blockman

pp **PROFESSOR M BLOCKMAN**
CHAIRPERSON, HSF HUMAN ETHICS
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.
The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

s.thomas

Part E

ANNEXURE 4

INSTITUTION AUTHORIZATION

TITLE OF THE RESEARCH PROJECT:	**Pre-hospital Discharge of Hypoglycemic Patients Post-Reversal**
REFERENCE NUMBER:	**BLYMOH001**
PRINCIPAL INVESTIGATOR:	**Mohamed Ridhaa Booley**
ADDRESS:	**University of Cape Town – Joint Division of Emergency Medicine**
CONTACT NUMBER:	**072 672 2223/ 021 938 6730**

To whom it may concern,

I ..... Dr. Cleave Robertson ..... representing the Western Cape Government Department of Health-Emergency Medical Services under his/her capacity as **Director: Western Cape Emergency Medical Services** - herewith authorize that this study be conducted in light of the principal investigator retrieving patient care report which will provide critical data to enable the administration of a telephonic interview for hypoglycaemic patients discharged in the pre-hospital setting. I also herewith authorize the principal investigator to make use of the Western Cape Emergency Medical Services contact centre in order to conduct a telephonic survey to meet the aims and objectives of the research project.

It is accepted by the principal researcher that all legal and ethical aspects of this study will be considered and mitigated as outlined in the presented study proposal and adhered to at all times.

Signed at (*place*) ..... Cape Town ..... On (7) ..... May ..... 2012.

....

Signature C. C. Robertson

Print Name in full

Part F

AFRICAN JOURNAL OF EMERGENCY MEDICINE

Produced on behalf of the African Federation for Emergency Medicine

AUTHOR INFORMATION PACK

TABLE OF CONTENTS

ISSN: 2211-419X

DESCRIPTION

The African Journal of Emergency Medicine (AfJEM) is the official journal of the *African Federation for Emergency Medicine*. It is an international, peer-reviewed journal aimed in particular at supporting emergency care across Africa. AfJEM publishes original research, reviews, brief reports of scientific investigations, case reports as well as commentary and correspondence related to topics of scientific, ethical, social and economic importance to emergency care in Africa. Articles will be of direct importance to African emergency care, but may have originated from elsewhere in the world.

AfJEM publishes manuscripts of international quality. This is ensured through a process of rigorous peer-review where manuscripts are evaluated for accuracy, novelty and importance. It is however recognised that African researchers in emergency care are disadvantaged in the available range of journals into which they can publish their work. The editorial team is aware that this is due to many reasons, including that developing world topics are often considered too basic for western Emergency Medicine journals, or that topics are concerned with conditions which are largely irrelevant to those audiences. Furthermore, the quality of submitted manuscripts is often lower than acceptable international journal standards due to inadequate research training. AfJEM is dedicated to support all authors who wish to make an attempt at publication on an African Emergency care topic. In order to maintain and produce a high quality, international standard Emergency Medicine journal, AfJEM has devised *Author Assist*. AfJEM uses a team of experienced volunteers to help improve the quality of manuscripts before peer-review submission. In this capacity AfJEM may, in suitable cases, be able to direct authors towards publication of suitably significant findings of an international interest in other international journals. AfJEM's *Author Assist* functions independently from peer-review and assistance rendered does not constitute an automatic indication of publication, but rather a process to improve an author's chances in succeeding at peer review.

AfJEM is uniquely tailored to the needs and requirements of emergency care workers dedicated to improving emergency medicine in Africa. It will be ideal reading material for physicians, nurses and pre-hospital care workers wishing to improve their knowledge on general emergency medicine, trauma care, paediatrics, injury and disease prevention, service improvement, policy and ethics, disaster preparedness and response, and all other aspects of emergency care. In keeping with the African Federation for Emergency Medicine, it is our aim to be recognised as the international voice of quality emergency medical care in Africa.

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TYPES OF ARTICLES
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Brief Research Reports: Reports of preliminary data and findings or studies with small numbers demonstrating the need for further investigation. References and a structured abstract are required. Maximum length: 1,500 words, plus the abstract (max 300 words) and references (max 10) and 3 tables and/or figures.

Concepts: Descriptions of clinical and nonclinical problems and solutions; descriptions of novel approaches to planning, management, or provision of emergency services; and practical "how-to" articles describing aspects of emergency medicine management. A narrative abstract is required. Maximum length: 3,000 words, plus the abstract (max 300 words) and references (max 50).

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Case Reports: Brief descriptions of a previously undocumented disease process, a unique unreported manifestation or treatment of a known disease process, or unique unreported complications of treatment regimens. Case reports should contain an introduction, narrative, and a discussion focusing on the implications of the case reported. They should not contain a review of the literature. Maximum length: 1,000 words, plus abstract (max 150 words) and references (max 10), and 1 table or figure.

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PREPARATION

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It is important that the file be saved in the native format of the wordprocessor used. The text should be in single-column format. Keep the layout of the text as simple as possible. Most formatting codes will be removed and replaced on processing the article. In particular, do not use the wordprocessor's options to justify text or to hyphenate words. However, do use bold face, italics, subscripts, superscripts etc. When preparing tables, if you are using a table grid, use only one grid for each individual table and not a grid for each row. If no grid is used, use tabs, not spaces, to align columns. The electronic text should be prepared in a way very similar to that of conventional manuscripts (see also the Guide to Publishing with Elsevier: http://www.elsevier.com/guidepublication). Note that source files of figures, tables and text graphics will be required whether or not you embed your figures in the text. See also the section on Electronic artwork.
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Divide your article into clearly defined and numbered sections. Subsections should be numbered 1.1 (then 1.1.1, 1.1.2, ...), 1.2, etc. (the abstract is not included in section numbering). Use this numbering also for internal cross-referencing: do not just refer to 'the text'. Any subsection may be given a brief heading. Each heading should appear on its own separate line.

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State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

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Provide sufficient detail to allow the work to be reproduced. Methods already published should be indicated by a reference: only relevant modifications should be described.

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A Theory section should extend, not repeat, the background to the article already dealt with in the Introduction and lay the foundation for further work. In contrast, a Calculation section represents a practical development from a theoretical basis.

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Results should be clear and concise.

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